

AMENDMENTS TO THE SPECIFICATION

Amendments to the specification are presented below with replacement paragraphs marked up to show changes made relative to the immediate prior version.

Please replace the first full paragraph on page 5 with the following amended paragraph:

It was believed that GBS toxin attacks the lungs of human neonates and binds embryonic neovasculature via receptors present on these tissues at birth and for a short time (about 7 days in term babies and longer in premature infants) thereafter. It was further hypothesized that the same receptors are present later in life only upon pathological neovasculature (i.e. new capillaries formed by pathological angiogenesis). This belief has been confirmed by the recent identification of novel proteins found on such cells that specifically bind GBS toxin. The nucleic acid and amino acid sequences of the human GBS toxin receptor known as HP59 are shown in SEQ ID NO: 1 AND SEQ ID NO: 2, respectively (~~GenBank~~GenBank[®] Accession Number AF244578). The nucleic acid and amino acid sequences of the sheep GBS toxin receptor known as SP55 (cloned from a sheep lung library, ~~GenBank~~GenBank[®] Accession Number AF244578) are shown in SEQ ID NO: 3 and SEQ ID NO: 4, respectively. Both HP59 and SP55 are integral proteins with multiple transmembrane domains. Each has several putative sites for phosphorylation by cAMP-dependent kinase, protein kinase (PKC) and casein kinase II (CK2) as well as putative sites for glycosylation and myristylation. Although HP59 has 41 amino acids at its amino terminus that SP55 lacks, the two proteins are otherwise 87% identical.

Please replace the last paragraph on page 11 and continuing onto page 12 with the following amended paragraph:

Antibodies to the GBS toxin receptor can be obtained by immunizing animals including rabbits, mice, goats and chickens with the GBS toxin receptor or an immunogenic fragment thereof. Monoclonal antibodies, polyclonal antibodies and variants thereof can be used. Examples of variants include, but are not limited to, single-chain (recombinant) antibodies, "humanized" chimeric antibodies, and immunologically active fragments of antibodies (e.g. Fab and Fab' fragments). The production of non-human monoclonal antibodies, e.g., murine, is well known (see, e.g., Harlow *et al*, *Antibodies A Laboratory Manual*, Cold Spring Harbor Press, pp. 139-240, 1989). Immunocompatible antibodies are preferred to prevent the immunized animal from mounting an immune response to the GBS toxin receptor antibodies. To prepare antibodies that are immunocompatible to a human, it is desirable to transfer antigen binding regions of non-human monoclonal antibodies, e.g. the F(ab')₂ or hypervariable regions of murine monoclonal antibodies, to human constant regions (Fc) or framework regions by recombinant DNA techniques to produce substantially human molecules. Such methods are generally known and are described in, e.g., U.S. Pat. Nos. 4,816,397 and 4,946,778, and EP publications 173,494 and 239,400. Alternatively, one may isolate DNA sequences which code for a human monoclonal antibody or portions thereof that specifically bind to the receptor protein by screening a DNA library from human B cells according to the general protocol outlines in WO 90/14430, and then cloning and amplifying the sequences which encode the antibody (or binding fragment) of the desired specificity.

These sequences may be inserted into the DNA of a mammal in such a manner that the mammal will secrete the antibodies into its milk (~~Genzyme Transgenics~~ Genzyme Transgenics[®], Framingham, MA). Such antibodies may be administered intraperitoneally or intravenously. Alternate regimens can be determined by one of skill in the art using the basic principles discussed under "Administration" below.

Please replace the third full paragraph on page 15 with the following amended paragraph:

In another embodiment, the GBS toxin receptor or polypeptide fragments from it can be synthesized chemically by techniques well known in the art, such as solid-phase peptide synthesis (Stewart et al., SOLID PHASE PEPTIDE SYNTHESIS, W.H. Freeman Co., San Francisco (1963)); Merrifield, *J. Am. Chem. Soc.* 85:2149-2154 (1963)). These and other methods of peptide synthesis are also exemplified by U.S. Patent Nos. 3,862,925, 3,842,067, 3,972,859, and 4,105,602. The synthesis can use manual synthesis techniques or automatically employ, for example, an ~~Applied BioSystems~~ Applied BioSystems[®] 430A or 431A Peptide Synthesizer (Forster City, California) following the instructions provided in the instruction manual supplied by the manufacturer.

Please replace the last paragraph on page 18 and continuing onto page 19 with the following amended paragraph:

Mammalian cell lines available as hosts for expression are known in the art and include many immortalized cell lines available from the ~~American Type Culture Collection~~

American Type Culture Collection[®] (ATCC), including, but not limited to, Chinese hamster ovary (CHO) cells, HeLa cells, baby hamster kidney (BHK) cells, monkey kidney cells (COS), N1E-115 (Liles *et al.*, *J. Biol. Chem.* 261:5307-5313, 1986), PC 12 human hepatocellular carcinoma cells (e.g., Hep G2), and a number of other cell lines, such as insect derived cell lines IF9 and IF21. Cell lines of particular preference are those expressing recombinant GBS toxin receptor constructs constitutively, lines which subsequently develop characteristics of a transformed cell, and lines that more preferably express GBS toxin receptor or fragments on the cell surface. Particularly preferred are ECV cells (a bladder carcinoma cell line originally referred to in the scientific literature as an endothelial cell line), human umbilical vein endothelial cells (HUVEC), bovine, sheep, and human adrenal medulla endothelial cells.